DEPARTMENT OF HEALTH & HUMAN SERVICES

New York District

Food & Drug Administration
158-15 Liberty Avenue
Jamaica, NY 11433

m379bn

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mary B. Harmon
Chairman of the Board and Senior Officer
Thames Pharmacal Co., Inc.
2100 Fifth Avenue
Ronkonkoma, NY 11779

May 5, 2000

Ref: NYK-2000-70

Dear Ms. Harmon:

During an inspection of your drug manufacturing facility located in Ronkonkoma, New York conducted on March 1 through April 5, 2000, our investigators documented deviations from the Current Good Manufacturing Practice for Finished Pharmaceuticals Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211). These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). The deviations include, but are not limited to, the following:

1. Failure to assure that your drug product bears a proper expiration date, determined by appropriate stability testing, so that it meets applicable standards of identity, strength, quality, and purity at the time of use as required by 21 CFR 211.137. For example, none of the annual stability batches for your product antipyrine and benzocaine otic solution, USP tested since 1996 (lot nos. K338, K739, M229, M305, and M326) have met the USP water specification throughout their labeled expiration period.

2. Failure to thoroughly investigate the failure of a distributed batch to meet any of its specifications and to prepare a written record of the investigation as required by 21 CFR 211.192. For example, the out-of-specification stability results for the above-mentioned batches of antipyrine and benzocaine otic solution, USP occurred in March through November 1999. There was no documented investigation of these failures including conclusions and follow-up actions.

3. Failure to have adequate written procedures to assure that each shipment of labeling and packaging materials is representatively sampled and examined upon receipt and before use as required by 21 CFR 211.122(a). For example, your firm's management was unaware of the source or rationale of its existing sampling plan for lithograph labeled tubes.

4. Failure to have adequate procedures that are used to reconcile the quantities of labeling issued, used, and returned to inventory as required by 21 CFR 211.125(c). For example, the discrepancy limit used by your firm for reconciling quantities of lithograph labeled tubes issued for individual packaging runs is excessively wide based on your firm's historical operating data.

5. Failure to assure that returned labeling is maintained and stored in a manner to prevent mix-ups and provide proper identification as required by 21 CFR 211.125(e). For example, our investigators observed that unused lithograph labeled tubes to be returned to inventory from packaging and labeling operations were being stored in an open area outside the packaging department. Further, our investigators observed that returned unused lithographed labeled tubes were not logged back into warehouse inventory in a timely manner. In addition, your firm's SOP requires warehouse personnel to double-check the accuracy of quantities of unused lithograph labeled tubes in opened cartons returned to inventory from packaging and labeling operations. There was no documentation that these checks were ever performed.

6. Failure to maintain adequate equipment usage logs as required by 21 CFR 211.182. For example, the [redacted] filling/packaging equipment usage log does not include an entry covering the use of this equipment in the packaging of triamcinolone acetonide cream USP, 0.1% (lot no. M793) into one ounce [redacted] lithograph labeled tubes, as indicated in the batch production records. (As you are aware, the above-mentioned batch of triamcinolone acetonide cream is the subject of an NDA-Field Alert Report and recall concerning your firm's mispackaging/mislabeling of some tubes of this product into lithograph labeled tubes labeled gentamicin sulfate ointment USP, 0.1%.)

7. Failure to properly identify processing lines used during the production of a batch of drug product to indicate their contents as required by 21 CFR 211.105(a). For example, the packaging line used during the processing of triamcinolone acetonide cream 0.1%, lot no. N229 did not identify the product and lot number.

8. Failure to have written procedures for and to document in the batch production records the visual examination of a representative sample of units collected at the completion of packaging and labeling operations for correct labeling as required by 21 CFR 211.134(b).

9. Failure to have written procedures for and to document in the batch production records the inspection of packaging and labeling facilities immediately after use to assure that packaging and labeling materials not suitable for subsequent operations have been removed as required by 21 CFR 211.130(e).

Neither the above identification of CGMP violations nor the inspectional observations (a copy of the Form FDA 483 is enclosed) presented to and discussed with you at the conclusion of the inspection is intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence with each requirement of the Act and its implementing regulations. The Food and Drug Administration (FDA) advises federal agencies of the issuance of all warning letters about drug products so that they may take this information into account when considering the award of contracts. Additionally, the FDA may not approve pending Antibiotic Form 6, NDA, ANDA, or export approval requests until the above violations are corrected.

You should take prompt action to correct these violations. Your failure to promptly correct these violations may result in regulatory action without further notice. These actions include, but are not limited to, seizure and injunction.

You should notify this office in writing, within 15 working days after receipt of this letter, of (1) each step that has been or will be taken to completely correct the current violations and to prevent the recurrence of similar violations; (2) the time within which the corrections will be completed; (3) any reason why the corrections have not been completed within the response time; and (4) any documentation necessary to show the corrections have been achieved.

You should send your reply to the attention of Bruce A. Goldwitz, Compliance Officer, Food and Drug Administration, 158-15 Liberty Avenue, Jamaica, NY 11433, Tel. (718) 340-7000 ext. 5582.

Sincerely,

Brenda J. Holman
District Director

Enclosure: Form FDA 483 dated April 5, 2000